

**REMARKS**

Claims 2-4 are pending in the present application. The claims are directed to a method for removing a TGF- $\beta$ .

In the Office Action, claims 2-4 remain rejected under 35 U.S.C. 103(a) as obvious over either of US 4774322 (Seyedin et al.), US 4931548 (Lucas) or US 5322933 (Davies), in view of US 6270994 (Miyazono). It is alleged in the Office Action that each of the first three references discloses isolating TGF- $\beta$  using reverse-phase chromatography with a C-18 column, and that the fourth cited reference provides a motivation to remove TGF- $\beta$  from body fluid because it discloses the presence of TGF- $\beta$  in body fluid associated with many conditions, so that it would have been obvious to remove TGF- $\beta$  from body fluid with a C-18 column chromatography.

In response to the argument made in the response to the first Office Action that the three first cited references only teach isolating TGF- $\beta$  from a purified TGF- $\beta$ -containing fraction, which is not indicative of whether TGF- $\beta$  would also be removed from body fluid, it is alleged in this Office Action that the teaching in the three first references that TGF- $\beta$  present in the particular fluids binds to a C-18 column is sufficient to provide an expectation that TGF- $\beta$  is also removed from other fluids, including body fluid.

Reconsideration and withdrawal of the rejection is respectfully traversed. The fluids from which TGF- $\beta$  is isolated in the cited references are considerably different from body fluid, and various column materials are used, so that these references provide no reasonable expectation that

TGF- $\beta$  could be successfully isolated from body fluid using the compound as recited in the present claims.

Specifically, even if it was considered, as alleged in the Office Action, that each the three first cited references "teaches removal from a tissue extract that would contain many other components," it cannot be controverted that each of these references teaches isolating TGF- $\beta$  by, first, processing and purifying a sample, and second, performing a step of isolating TGF- $\beta$ . There is no suggestion in any of these references that the steps of processing and purifying the sample could be dispensed with. Therefore, even if, arguendo, a person of ordinary skill in the art would attempt to remove TGF- $\beta$  from body fluid, that person would find no suggestion or motivation in the three first cited references to contact a body fluid with the adsorbent, but would find a clear teaching that a preliminary sample preparation and purification step is required before attempting TGF- $\beta$  removal.

In addition, even though the samples from which TGF- $\beta$  is isolated in the three first cited references might contain other components, it is also understood that the sample preparation and purification steps taught in these references have removed large numbers and amounts of components. Further, successful TGF- $\beta$  isolation in the presence of certain components remaining in the purified samples, as suggested by the cited references, does not in itself provide an expectation that TGF- $\beta$  isolation would also have succeeded in the presence of different types or amounts of components, if such components had not been removed by the preliminary preparation and purification steps taught in these references. As a result, a person of ordinary skill in the art

would have no reasonable expectation of success if that person attempted removal of TGF- $\beta$  from body fluid by bringing a body fluid into contact with an adsorbent as recited in present claim 4.

Also, at least the Lucas reference teaches the use of Synchronapak C4 column for RP-HPLC (see Lucas from col. 3, line 57 to col. 4, line 27). Synchronapak C4 material generally has a log P of less than 2.5 even if various kinds of functional groups are considered. Therefore, even if, still arguendo, a person of ordinary skill in the art would attempt to remove TGF- $\beta$  from body fluid, that person would find no suggestion or motivation in the cited references to remove TGF- $\beta$  from body fluid by selectively using a compound having a log P value of at least 2.50, since at least Lucas suggests using another type of compound.

In contrast, the present inventors have unexpectedly discovered that TGF- $\beta$  can be removed from body fluid by bringing a body fluid into contact with an adsorbent comprising (i) a water-insoluble carrier, and (ii) a compound immobilized on said carrier and having a log P value of at least 2.50, as recited in present claim 4. This feature of the present claims is not taught or suggested in any of the cited references, because they fail to establish (i) a connection between removal of a compound from a purified or high-concentration fluid and removal of the compound from a non-purified or low-concentration fluid, or (ii) a connection between the log P value of a compound and TGF- $\beta$  removal effect. Therefore, the present claims are not obvious over any combination of the cited references.

In view of the above, it is submitted that the rejection should be withdrawn.

Serial Number: 09/773,598

Group Art Unit: 1646


In conclusion, the invention as presently claimed is patentable. It is believed that the claims are in allowable condition and a notice to that effect is earnestly requested.

In the event there is, in the Examiner's opinion, any outstanding issue and such issue may be resolved by means of a telephone interview, the Examiner is respectfully requested to contact the undersigned attorney at the telephone number listed below.

In the event this paper is not considered to be timely filed, the Applicants hereby petition for an appropriate extension of the response period. Please charge the fee for such extension and any other fees which may be required to our Deposit Account No. 01-2340.

Respectfully submitted,

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NES:rep  
Encl.: Petition for One-Month Extension of Time